PCT application WO 94/02602, published 3 February 1994 and incorporated herein at pages 39-141, describes in detail the production of transgenic nonhuman animals which are modified so as to produce antibodies with fully human variable regions rather than endogenous antibodies in response to antigenic challenge. Briefly, the endogenous loci encoding the light and heavy immunoglobulin chains are incapacitated in the transgenic hosts and loci encoding human heavy and light chain proteins are inserted into the genome. In general, the animal which provides all the desired modifications is obtained by cross-breeding intermediate animals containing fewer than the full complement of modifications. The preferred embodiment of the nonhuman animal described in the specification is a mouse. Thus, mice, specifically, are described which, when administered immunogens, produce antibodies with human variable regions, including fully

Replace the paragraph on page 2, lines 14-18 with the following paragraph.

The availability of the nonhuman, immunogen-responsive transgenic animals described in the above-referenced WO 94/02602, which is incorporated herein at pages 39-141, makes possible convenient production of human antibodies without the necessity of employing human hosts.

Replace the paragraph on page 8, lines 3-5 with the following paragraph.

The details for constructing such an animal useful in the method of the invention are provided in the PCT application WO 94/02602 referenced above and incorporated herein at pages 39-141.

Replace the paragraph on page 20 beginning at line 18 down to line 31 (the last line on the page) with the following paragraph.

In these examples, mice, designated "xenomice", are used for initial immunizations. A detailed description of such xenomice is found in the above-referenced PCT application WO 94/02602, which is incorporated herein at pages 39-141. Immunization protocols appropriate to each antigen are described in the specific examples below. The sera of the immunized xenomice (or the supernatants from immortalized B cells) were titrated for antigen specific human antibodies in each case using a standard ELISA format. In this format, the antigen used for immunization was immobilized onto wells of microtiter plates. The plates were washed and blocked and the sera (or supernatants) were added as serial dilutions for 1-2 hours of incubation. After washing, bound antibody having human characteristics was

IN THE CLAIMS

Cancel claim 1, without prejudice, replace pending claims 2 and 3 with claims 2 and 3 below, and add claims 46 and 47.

2. The method according to claim 46 or 47, wherein said recovering step comprises recovering polyclonal immunoglobulin from said transgenic mouse.

3. The method according to claim 46 or 47, wherein said recovering step comprises immortalizing B cells from said transgenic mouse immunized with said antigen, screening the resulting immortalized cells for the secretion of said immunoglobulin specific for said antigen, and